Robust 7T Spin Echo BOLD fMRI using Subject-Tailored Multidimensional Excitation and Refocusing Pulses

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Target Audience: Imaging scientists with an interest in high field quantitative functional brain imaging

Purpose: *The purpose of this study is to develop and implement tailored radiofrequency (RF) excitation and refocusing pulses at 7T to allow for robust detection of R_2-weighted spin echo (SE) blood oxygenation level-dependent (BOLD) activity in multiple brain regions.* BOLD functional MRI (fMRI) contrast is derived from changes in R_2(*) dephasing of water through local field gradients that adjusts during periods of altered hemodynamic (cerebral blood flow: CBF; cerebral blood volume: CBV) and metabolic (cerebral metabolic rate of oxyben: CMR_{O2}) demand. The majority of BOLD studies utilize gradient echo (GRE) readouts, owing to the high contrast-to-noise ratio (CNR), however GRE BOLD is extremely sensitive to B_0 inhomogeneity, local susceptibility changes, and vessel orientation and geometry. Variability in BOLD contrast can be reduced by (i) imaging at high field (e.g., 7T) where intravascular (IV) effects are negligible at intermediate TE~tissue $T_2^{(*)}=1/R_2^{(*)}$, and (ii) by performing R_2-weighted SE BOLD, which refocuses dephasing due to static field heterogeneity[1]. 7T SE BOLD holds great potential for quantitative physiology, as unlike R_2*, R_2 can be directly related to extravascular changes secondary to CBF, CBV and CMR_{O2} dynamics[2]. However, 7T SE BOLD is generally only performed over limited field of views and/or with specialized coils due to the high power and suboptimal refocusing pulse performance. Here, we implement tailored RF excitation and refocusing at 7T using commercially available transmit and receive coils and demonstrate robust 7T SE BOLD fMRI improvements in sensitivity and CNR.

Methods: *Development.* The goal of subject-tailored multidimensional excitation is to produce a flip angle pattern that cancels spatial variations in B_1^+. The advantage of tailored pulses over adiabatic pulses conventionally used to mitigate B_1^+ nonuniformities is that, while they require subject-specific measurements and pulse computations, they generally have much lower SAR. In this work, two tailored pulse types were used: spokes pulses[3] for excitation and k_T-points pulses[4] for refocusing. Spokes pulses are based on a multidimensional excitation k-space trajectory that enables simultaneous excitation of a sharp slice profile, and a smooth in-plane profile that cancels expected smooth variations in B_1^+, while k_T-points pulses are a non-slice-selective variant of spokes pulses. After acquiring subject-specific B_1^+ and B_0 maps, the tailored pulses in this study were designed using a joint large-tip-angle multidimensional RF and gradient design algorithm[5]. *Experiment.* Implementation was evaluated at 7T (Philips Medical Systems) using single-channel birdcage head coil transmit and 32-channel SENSE receive coil (n=4; age=32+/-8 yrs; 3M/1F) who provided informed, written consent. A T_1-weighted localizer, and B_0 and B_1+ field map were obtained, followed by BOLD fMRI (1.6x1.6x2 mm^3) for (i) GRE (TR/TE=3000/25 ms), (ii) non-tailored SE (SE_{NTRF}) using a time-bandwidth 4, 5.3 ms sinc excitation and 1.4 ms composite refocusing pulses (TR/TE=3000/50 ms), and (iii) tailored SE using 3-spoke excitation (duration~11 ms; nominal peak B_1~9 μT) and 5-k_T-points refocusing (duration~5 ms; nominal peak B_1~7.5 μT) tailored to the subject B_1^+ maps (SE_{TRF}). SE_{TRF} SAR was lower than that of the (product) SE_{NTRF} sequence; the minimum TR of the SE_{NTRF} sequence was 392 ms, while the SE_{TRF} sequence had a minimum TR of 136 ms. Each acquisition was performed during a breath hold task with imaging volume centered on temporal lobe and for a neuronal (finger tapping) task for a slice centered on M1. Motor task: 21s/12s off/on (repetitions=3) 1 Hz finger tapping; breath hold: 42s/15s off/on (repetitions=5). *Analysis.* Data were corrected for motion and baseline drift and activation maps (z>4.0; P<0.05) were calculated using standard multiple regression and non-parametric autocorrelation routines. To prevent sensitivity bias to draining veins which are expected to provide different contrast in SE vs. GRE, a region-of-interest in cortical gray matter (breath hold) and in M1 (finger tapping), was drawn and regions of large veins, were excluded. For mean signal, S; signal change ΔS; and standard deviation of signal across all measurements, σ; timecourse SNR (S/σ) and CNR ($\Delta S/\sigma$) were calculated for each sequence and task.

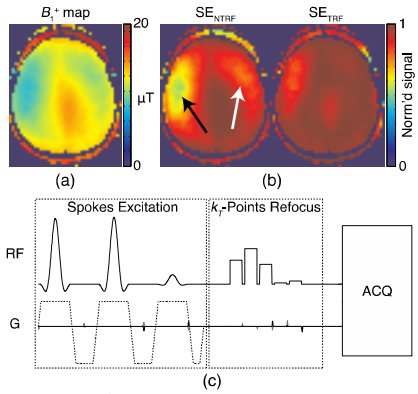

Fig 1. (a) B_1^+ map measured in subject from Fig. 2. This map and a B_0 map were used in the design of tailored spokes and k_T-points pulses. (b) Predicted normalized signal patterns for the SE_{NTRF} and SE_{TRF} sequences. The tailored excitations result in signal recovery in right (black arrow, ~50% higher signal) and left (white arrow, ~30% higher signal) hemispheres. (c) Tailored SE pulse sequence, with a 3-spoke excitation and 5-k_T-points refocusing pulses.

Results and Discussion: Total pulse computation time was approximately 19s. For the motor task, activation maps showed a significant (P<0.05) increase in spatial sensitivity to the functional region in the SE_{TRF} approach relative to the SE_{NTRF} approach (*Fig. 2*). 143 activated voxels (z>4.0) for the SE_{TRF} vs. 110 for the SE_{NTRF} approach were found (30% increase). However, many (n=53) of the SE_{NTRF} voxels were spuriously located outside motor cortex; when this was taken into account, the SE_{TRF} approach provided an increase in voxel detection specificity of approximately 150%. CNR (GRE: 2.1; SE_{NTRF}=0.74; SE_{TRF}=1.13) was also significantly increased (P<0.05) by an average of 52% in SE_{TRF} vs. SE_{NTRF}. SE_{TRF} voxels were found to more closely co-localize with cortex, whereas while more robust, GRE activation co-localized additionally with CSF and tissue surrounding large veins, consistent with static refocusing and dynamic averaging of field inhomogeneities within and around large vessels in SE. The benefit of the tailored approach was even more substantial when more inferior images in temporal lobe were considered, where field inhomogeneity is higher. Here, in response to the breath hold challenge, total cortical activated voxels were found to be 1718, 849, and 356 for GRE, SE_{TRF}, and SE_{NTRF}, respectively (138% increase in activated voxels in SE_{TRF} vs. SE_{NTRF}). GRE (CNR=2.9) and SE_{TRF} (CNR=0.3) provided positive, robust reactivity, whereas SE_{NTRF} CNR was not statistically different from zero. As expected, CNR was reduced in the SE approaches relative to GRE, owing to the added sensitivity of GRE BOLD to extravascular R_2* changes around large veins. Note that our analysis approach excludes large veins, resulting in CNR values lower than those reported in some other studies.

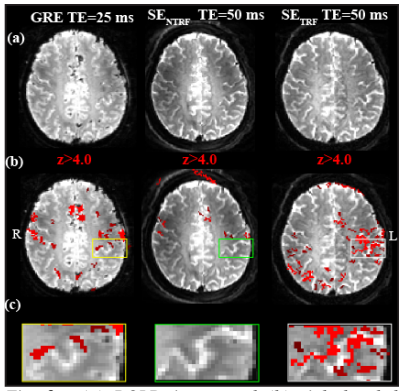

Fig. 2. (a) BOLD image and (b) right-handed finger-tapping activation map overlaid for GRE, non-tailored SE (SE_{NTRF}) and tailored SE (SE_{TRF}). Note the increase in signal intensity in bilateral M1 regions in SE_{TRF} vs. SE_{NTRF}, which (c) translates to improved spatial specificity for stimulus-induced activation in left M1.

Conclusions: An improvement in spatial specificity and CNR was demonstrated for 7T SE BOLD performed using tailored spokes and k_T point refocusing pulses compared with a standard sequence using sinc-excitation and composite refocusing. Tailored RF pulses, which can be generated quickly from session-specific B_0 and B_1^+ maps therefore have great potential for 7T SE BOLD, which should evince more quantitative and stable investigations of physiology between populations and over time.

References: [1]Yacoub E, et al. Neuroimage. 2007 Oct 1;37(4):1161-77. [2]van Zijl PC, et al. Nat Med. 1998 Feb;4(2):159-67. [3]Saekho S, et al. MRM. 2006;55(4):719-24. [4]Cloos MA, et al. MRM. 2011;67:72-80. [5]Grissom WA, et al. ISMRM 2010, p. 99.